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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,814	08/26/1998	MASAHIKO DOHI	Q51505	8214

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EXAMINER	
BERMAN, ALYSIA	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 05/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/125,814	Applicant(s) DOHI ET AL.	
	Examiner Alysia Berman	Art Unit 1617	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Receipt is acknowledged of the amendment and declaration filed October 22, 2001. Claims 19-32, 34 and 36-45 have been canceled. Claims 46 and 48-50 have been amended. Claims 51-98 have been added.

Election/Restrictions

2. Upon further review of the claims and in view of applicants' arguments, the election of species requirement is withdrawn because all of the claims are drawn to a product. All of the claims have been examined.

Drawings

3. The drawings filed on August 26, 1998 has been received and approved by the Draftsperson.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 51-98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 51-98 are indefinite because of the term "described" in line one of the claims. It is unclear if Applicant intends to claim the composition of the base claims or a composition like the base claims. Amendment of the claims substituting "according to" for "described in" would overcome this rejection.

7. Claims 51-54, 75-77 and 95-98 recite the limitation "the particles" or "the resultant particles" or "the average particle diameter". There is insufficient antecedent basis for this limitation in the claim. None of the base claims recite particles.

8. Claims 55, 56, 76, 77, 79, 80 and 95-98 are indefinite because it is unclear to which particles the claims are referring. Does Applicant intend that the average particle diameter of each component be based on the total amount of particles or on the amount of particles of each component, respectively?

9. Claims 58 and 82 are indefinite because it is unclear what Applicant intends by "vitamin preparations". Vitamin preparations are not clearly defined by the claims or the specification. The metes and bounds of the claims cannot be determined.

10. Claims 59, 61, 63, 83, 85 and 87 are indefinite because they recite the term derivatives. This term is not clearly defined as it pertains to each of the components claimed. The metes and bounds of the claims cannot be determined.

term of Art → 11. Regarding claims 59, 63, 83 and 87, the phrase "insulin-like" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

12. The term "vigorously" in claims 51, 68, 75 and 92 is a relative term that renders the claims indefinite. The term "vigorously" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

13. Claims 54 and 78 are indefinite because it is unclear what part of the water-absorbing and gel-forming base material the average particle diameter of the water-absorbing and water-insoluble base material is larger than. Does Applicant intend to claim that the average particle diameter of the water-absorbing and water-insoluble base material is larger than the average particle diameter of the water-absorbing and gel-forming base material?

14. This application is replete with 35 U.S.C. 112 issues. The above are just some examples. Applicant is required to review all of the claims for 35 U.S.C. 112, 2nd paragraph issues and make appropriate corrections.

15. All claims that depend from rejected base claims are also rejected as indefinite.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. The claims as written are all drawn to the product of a powdery composition. None of the claims as written are drawn to proper product-by-process claims because none of them recite positive steps of making the product.

19. Claims 46-57, 59-81 and 83-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (US 4,613,500).

Suzuki teaches all of the limitations of the claims as stated in paper no. 23. Suzuki is directed to a powdery composition for nasal administration that contains a polypeptide, a water-absorbing and water-insoluble base material and, optionally, a water-absorbing and water-soluble (gel-forming) base material (title, abstract and col. 4, lines 50-66). For crystalline cellulose, *inter alia*, as the water-insoluble base, see col. 4, lines 21-41. For hydroxypropyl cellulose, *inter alia*, as the water-soluble (gel-forming) base, see column 5, lines 10-22. The amount of gel-forming base is from 0.1-60 wt.% based on the amount of water-insoluble base (col. 5, lines 22-25).

Suzuki discloses at column 5, lines 53-65 that the drug may be adhered to or dispersed in the water-insoluble base. Suzuki does not teach that the drug is adhered to or dispersed in the gel-forming base. Therefore, even with the addition of a gel-forming base, it is reasonable to expect that the drug would be more adhered to or dispersed in the water-insoluble base. The particle size of more than 90 wt.% of the resultant particles is 10-250 microns (col. 5, lines 26-28). This suggests that the average particle size of each component, water-insoluble base, gel-forming base and drug, is 10-250

microns, which is encompassed by or overlaps the instantly claimed particle size ranges. The molecular weight of the polypeptide used is from 1,000 to 300,000, preferably 1,000 to 150,000 (col. 2, lines 56-63).

Suzuki does not teach the amount of drug dispersed on or in the base materials or the viscosity of the hydroxypropyl cellulose. It is within the skill in the art to select optimal parameters in a composition in order to achieve a beneficial effect. *In re Boesch*, 205 USPQ 215 (CCPA 198). Therefore, absent evidence of unexpected results, the amount of drug dispersed on or in the base materials is not given patentable weight. Suzuki does not limit the viscosity of the hydroxypropyl cellulose used. Therefore, the disclosure of Suzuki encompasses hydroxypropyl cellulose with a viscosity as instantly claimed. Absent evidence of unexpected results obtained by using hydroxypropyl cellulose with the instantly claimed viscosity, this limitation is not considered critical to the invention.

Although the claims recite process steps for achieving uneven drug dispersion, they are drawn to compositions. The claims do not recite process steps for making the final product. The process by which a product or any part thereof is obtained does not render claims to the product patentable over the prior art.

It would have been obvious to one of ordinary skill in the art at the time of the invention to select an optimal amount of drug dispersed on or in the base materials, an optimal viscosity of hydroxypropyl cellulose and disperse or adhere the drug more on or in the water-insoluble base material in the compositions of Suzuki in order to obtain a sufficient dose of drug with increased absorption efficiency.

20. Claims 58 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. as applied to claims 46-57, 59-81 and 83-98 above, and further in view of Makino et al. (US 5,262,871).

Suzuki teaches all the limitations of the claims as stated in the 35 U.S.C. 103(a) rejection above.

It does not teach a non-peptide/non-proteinaceous drug. Makino discloses non-peptide/non-proteinaceous drugs (col. 7, line 60 to col. 8, line 26) for use in powdery nasal compositions (col. 4, lines 11-13).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a non-peptide/non-proteinaceous drug as taught by Makino in the composition of Suzuki expecting to obtain sufficient absorption of the drug through the nasal mucosa.

Response to Arguments

21. Applicant's arguments filed October 22, 2001 have been fully considered but they are not persuasive.

22. Applicant argues that the term "insulin-like growth factors" is a well-known term of art. Applicant has not provided any information to show that one skilled in the art would understand what Applicant intends by this term. It is noted that Applicant refers to pages from *Products for Life Science Research* that were submitted with the amendment filed October 22, 2001. However, no such reference was found in the file.

23. Applicant argues that Suzuki does not teach or suggest a composition containing both a water-absorbing and water-insoluble base material and a water-absorbing and

gel-forming base material where the drug is unevenly dispersed more on or in the water-absorbing and water-insoluble base material. The declaration filed October 22, 2001 has been considered but is not found persuasive. As stated in paper no. 23 and above, Suzuki teaches that the drug can be either adhered to or dispersed in the water-absorbing and water-insoluble base material (col. 5, lines 53-65). Suzuki does not disclose or suggest that the drug is adhered to or dispersed in the water-absorbing and gel-forming base material. Therefore, one of ordinary skill in the art would expect the drug to be adhered to or dispersed in the water-absorbing and water-insoluble base material in the composition of Suzuki.

The declaration is not commensurate in scope with the instant independent claims. The declaration asserts unexpected results when the particles are processed in a particular manner. However, the claims as written do not require process steps for making the product. Additionally, the declaration does not provide clear evidence that the instantly claimed invention obtains unexpected results over the prior art. Burden is on Applicant to establish unexpected results and clearly explain any data presented. See MPEP §716.02(b). There is no clear nexus between the AUC measured and the estimated ratio of the amount of drug adhered to the water-insoluble base. It is unclear how the AUC data provided in the declaration can be taken to show unexpected results of amount of drug adhered to the water-insoluble base.

Additionally, it is not clear how a greater adherence of the drug to the water-insoluble base or an increased bioavailability of drug is unexpected over the prior art. The prior art teaches both adherence of the drug to the water-insoluble base and that

the water-insoluble base provides increased absorption efficiency of the drug through the nasal mucosa (col. 3, line 63 to col. 4, line 12). Applicant has not provided data showing a significant difference of unexpected results between the instant invention and the prior art.

24. Applicant argues that Makino does not make up the deficiencies of Suzuki because Makino does not teach or suggest a powdery composition where a drug is unevenly dispersed more on or in a water-absorbing and water-insoluble base material than on or in a water-absorbing and gel-forming base material. As stated in the 35 U.S.C. 103(a) rejection above, it is the Examiner's position that Suzuki does teach uneven dispersion of the drug more on or in a water-absorbing and water-insoluble base material than on or in a water-absorbing and gel-forming base material. Makino is used merely to show that it is known in the art to use non-peptide/non-proteinaceous drugs in powdery nasal compositions. Therefore, the combination of Suzuki and Makino teach a powdery nasal composition containing a non-peptide/non-proteinaceous drug, a water-insoluble base material and a gel-forming base material where the drug is unevenly dispersed more on or in the water-insoluble base material than the gel-forming base material.

25. It appears as if Applicants' invention lies in products that are made by particular processes. However, applicant has not presented proper product-by-process claims. The steps recited by claims 67-74 and 91-98 are directed to achieving uneven drug dispersion, not making the final product.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alysia Berman whose telephone number is 703-308-4638. The examiner can normally be reached Monday through Friday between 9:00 am and 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, can be reached on 703-308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 or 703-872-9307 for after-final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234 or 703-308-1235.

Alysia Berman
Patent Examiner
May 10, 2002

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